

What is claimed is:

1. An isolated or purified peptide comprising an amino acid sequence selected from the group consisting of:

(a)

GPRGPPGPPGKPGDDGEAGKPGKSGERGPPGPQGARGFPGTPGLPGVKGHR  
GYPLDGAKEAGAPGVKGESGSPGQNGSPGGPM (CB12);

(b) GPRGPPGPPGKPGDDGEAGKPGKSGERGPPG (CB12-I);

(c) ERGPPGPQGARGFPGTPGLPGVK (CB12-II);

(d) GLPGVKGHRGYPLDGAKEAGAPG (CB12-III);

(e) GEAGAPGVKGESGSPGQNGSPGPM (CB12-IV);

(f) GERGPPGPQGARGFP\*GTP\*GLP\*GVK wherein the \* denotes sites of hydroxylation. (Pro6);

(g) GERGPP\*GPQGARGFPGTP\*GLP\*GVK wherein the \* denotes sites of hydroxylation. (Pro15);

(h) GERGPP\*GPQGARGFP\*GTPGLP\*GVK wherein the \* denotes sites of hydroxylation. (Pro18); and

(i) GERGPP\*GPQGARGFP\*GTP\*GLPGVK wherein the \* denotes sites of hydroxylation. (Pro21)

or a fragment or conservatively substituted variant thereof, wherein said peptide is effective in altering the rate of degradation of type II collagen or the rate of chondrocyte hypertrophy.

2. The peptide fragment of claim 1, wherein said peptide is further modified by hydroxylation.

3. The peptide fragment of claim 2, wherein said peptide is hydroxylated at one or more of the proline or lysine residues of said peptide.

4. The peptide fragment of claim 3, wherein said peptide is hydroxylated at one or more proline residues located within the sequence Gly-X-Pro, where X indicates any amino acid.

5. The peptide fragment of claim 3, wherein said peptide is hydroxylated at one or more lysine residues located within the sequence Gly-X-Lys, where X indicates any amino acid.

6. A peptide fragment consisting essentially of an amino acid sequence denoted CB12:  
GPRGPPGPPGKPGDDGEAGKPGKSGERGPPGPQGARGFPGTPGLPGVKGHRGY  
PGLDGAKEAGAPGVKGESGSPGQNGSPGGPM.

7. The peptide fragment of claim 6, wherein said peptide is further modified by hydroxylation.

8. The peptide fragment of claim 7, wherein said peptide is hydroxylated at one or more of the proline or lysine residues of the peptide.

9. The peptide fragment of claim 8, wherein said peptide is hydroxylated at one or more proline residues located within the sequence Gly-X-Pro, where X indicates any amino acid.

10. The peptide fragment of claim 8, wherein said peptide is hydroxylated at one or more lysine residues located within the sequence Gly-X-Lys, where X indicates any amino acid.

11. The peptide fragment of claim 7, wherein said peptide consists essentially of  
GPRGPP\*GPP\*GKP\*GDDGEAGKP\*GKSGERGPP\*GPQGARGFP\*GTP\*GLP\*GV  
KGHRGY PGLDGAKEAGAP\*GVKGESGSP\*GQNGSP\*GGPM and wherein the \* denotes sites of hydroxylation.

12. A mimetic of said peptide fragment of claim 6.
13. A mimetic of said peptide fragment of claim 11.
14. An inhibitor of said peptide fragment of claim 6.
15. An inhibitor of said peptide fragment of claim 11.
16. A peptide fragment consisting essentially of an amino acid sequence denoted CB12-II: GERGPPGPQGARGFPGTPGLPGVK.
17. The peptide fragment of claim 16, wherein said peptide is further modified by hydroxylation.
18. The peptide fragment of claim 17, wherein said peptide is hydroxylated at one or more of the proline or lysine residues of the peptide.
19. The peptide fragment of claim 18, wherein said peptide is hydroxylated at one or more proline residues located within the sequence Gly-X-Pro, where X indicates any amino acid.
20. The peptide fragment of claim 18, wherein said peptide is hydroxylated at one or more lysine residues located within the sequence Gly-X-Lys, where X indicates any amino acid.
21. The peptide fragment of claim 17, wherein said peptide consists essentially of GERGPP\*GPQGARGFP\*GTP\*GLP\*GVK.
22. A mimetic of said peptide fragment of claim 16.
23. A mimetic of said peptide fragment of claim 21.
24. An inhibitor of said peptide fragment of claim 16.
25. An inhibitor of said peptide fragment of claim 21.

26. The peptide fragment of claim 16, wherein said peptide consists essentially of GERGPPGPQGARGFP\*GTP\*GLP\*GVK (Pro6) and wherein the \* denotes sites of hydroxylation.

27. A mimetic of said peptide fragment of claim 26.

28. An inhibitor of said peptide fragment of claim 26.

29. The peptide fragment of claim 16, wherein said peptide consists essentially of GERGPP\*GPQGARGFPGTP\*GLP\*GVK (Pro15) and wherein the \* denotes sites of hydroxylation.

30. A mimetic of said peptide fragment of claim 29.

31. An inhibitor of said peptide fragment of claim 29.

32. The peptide fragment of claim 16, wherein said peptide consists essentially of GERGPP\*GPQGARGFP\*GTPGLP\*GVK (Pro18) and wherein the \* denotes sites of hydroxylation.

33. A mimetic of said peptide fragment of claim 32.

34. An inhibitor of said peptide fragment of claim 32.

35. The peptide fragment of claim 16, wherein said peptide consists essentially of GERGPP\*GPQGARGFP\*GTP\*GLPGVK (Pro21) and wherein the \* denotes sites of hydroxylation.

36. A mimetic of said peptide fragment of claim 35.

37. An inhibitor of said peptide fragment of claim 35.

38. A peptide fragment consisting essentially of an amino acid sequence denoted as CB12-I: GPRGPPGPPGKPGDDGEAGKPGKSGERGPPG.

39. The peptide fragment of claim 38, wherein said peptide is further modified by hydroxylation.

40. The peptide fragment of claim 39, wherein said peptide is hydroxylated at one or more of the proline or lysine residues of the peptide.

41. The peptide fragment of claim 40, wherein said peptide is hydroxylated at one or more proline residues located within the sequence Gly-X-Pro, where X indicates any amino acid.

42. The peptide fragment of claim 40, wherein said peptide is hydroxylated at one or more lysine residues located within the sequence Gly-X-Lys, where X indicates any amino acid.

43. The peptide fragment of claim 38, wherein said peptide consists essentially of GPRGPP\*GPP\*GKP\*GDDGEAGKP\*GKSGERGPP\*G and wherein the \* denotes sites of hydroxylation.

44. A mimetic of said peptide fragment of claim 38.

45. An inhibitor of said peptide fragment of claim 38.

46. A mimetic of said peptide fragment of claim 43.

47. An inhibitor of said peptide fragment of claim 43.

48. A peptide fragment wherein said peptide consists essentially of an amino acid sequence denoted as CB12-III: GLPGVKGHRGYPLDGAKEAGAPG.

49. The peptide fragment of claim 48, wherein said peptide is further modified by hydroxylation.

50. The peptide fragment of claim 49, wherein said peptide is hydroxylated at one or more of the proline or lysine residues of the peptide.

51. The peptide fragment of claim 50, wherein said peptide is hydroxylated at one or more proline residues located within the sequence Gly-X-Pro, where X indicates any amino acid.

52. The peptide fragment of claim 50, wherein said peptide is hydroxylated at one or more lysine residues located within the sequence Gly-X-Lys, where X indicates any amino acid.

53. The peptide fragment of claim 48, wherein said peptide consists essentially of GLP\*GVKGHRGYP\*GLDGAKGEAGAP\*G and wherein the \* denotes sites of hydroxylation.

54. A mimetic of said peptide fragment of claim 48.

55. An inhibitor of said peptide fragment of claim 48.

56. A mimetic of said peptide fragment of claim 53.

57. An inhibitor of said peptide fragment of claim 53.

58. A peptide fragment consisting essentially of an amino acid sequence denoted as CB12-IV: GEAGAPGVKGESGSPGQNGSPGPM.

59. The peptide fragment of claim 58, wherein said peptide is further modified by hydroxylation.

60. The peptide fragment of claim 59, wherein said peptide is hydroxylated at one or more of the proline or lysine residues of the peptide.

61. The peptide fragment of claim 60, wherein said peptide is hydroxylated at one or more proline residues located within the sequence Gly-X-Pro, where X indicates any amino acid.

62. The peptide fragment of claim 60, wherein said peptide is hydroxylated at one or more lysine residues located within the sequence Gly-X-Lys, where X indicates any amino acid.

63. The peptide fragment of claim 58, wherein said peptide consists essentially of GEAGAP\*GVKGESGSP\*GQNGSP\*GPM and wherein the \* denotes sites of hydroxylation.

64. A mimetic of said peptide fragment of claim 58.
65. An inhibitor of said peptide fragment of claim 58.
66. A mimetic of said peptide fragment of claim 63.
67. An inhibitor of said peptide fragment of claim 63.
68. A peptide as in any one of claims 1, 6, 16, 38, 48 or 58, wherein 1-5 acids of the peptide sequence have been replaced using conservative substitutions and wherein said peptide is effective in altering the rate of degradation of type II collagen or the rate of chondrocyte hypertrophy.
69. A peptide which has at least 80% homology to a peptide as in any one of claims 1, 6, 16, 38, 48 or 58, and wherein said peptide is effective in altering the rate of degradation of type II collagen or the rate of chondrocyte hypertrophy.
70. A peptide dimer consisting of two peptides wherein each peptide is selected from the group of peptides in claim 1.
71. The peptide dimer of claim 70, wherein said peptide dimer is a homodimer or a heterodimer.
72. A peptide trimer consisting of three peptides wherein each peptide is selected from the group of peptides of claim 1.
73. The peptide trimer of claim 72, wherein said peptide trimer is a homotrimer or a heterotrimer.
74. A pharmaceutical composition comprising a pharmaceutically effective carrier and at least one of the inhibitors of any one of claims 14, 15, 24, 25, 28, 31, 34, 37, 45, 47, 55, 57, 65, or 67.
75. Use of a pharmaceutical composition as in claim 74, wherein said composition reduces collagen matrix turnover in mammals.

76. Use of a pharmaceutical composition according to claim 74, wherein said composition reduces collagen matrix turnover in humans.

77. A method of regulating collagen turnover comprising:  
  
administering to a subject a pharmaceutically effective amount of said pharmaceutical composition according to claim 74.

78. Use of a pharmaceutically effective dose of said pharmaceutical composition of according to claim 74, wherein the administration of said composition reduces degradation of one or more collagen proteins.

79. A method of identifying a peptide mimetic of a peptide fragment of collagen capable of decreasing the degradation of the collagen in a biological sample comprising:

(a) screening peptide fragments of collagen, and variants thereof for the ability of the peptide fragments to bind preferentially to a specific receptor of the naturally produced peptide fragments but has a lesser ability to activate the matrix degradation pathway.

80. The method of claim 79, wherein said specific receptors are anti-integrin receptors.

81. The method of claim 79, wherein said activation of the matrix degradation pathway induces the expression of genes selected from the group consisting of COLX, MMP-9, TGF-B1, IHH, MMP-13, CBFA1, SOX 9, bFGF, pTHrP, caspase-3, MT1-MMP, IL-1B, and MMP-1.

82. The method of claim 79, wherein said biological sample is a biological fluid selected from the group consisting of tissue extracts, synovial fluid, serum and urine.

83. An isolated or purified antibody that specifically binds to an epitope of said peptide or an antigenic fragment thereof as in claims 1, 6, 16, 38, 48 or 58.



84. The antibody of claim 83, wherein said antibody is a monoclonal or a polyclonal antibody.

85. The antibody of claim 83, wherein said antibody is used to inhibit the activity of said peptide.

86. The antibody of claim 83, wherein said antibody is used to identify inhibitors of the generation of said peptide.

87. The antibody of claim 83, wherein said antibody is used to identify a subject at risk for rapid or slow progression of a disease, responding to therapy designed to arrest cartilage degradation or at risk for a disease by showing of early pre-clinical changes prior to clinical presentation of said disease.

88. The antibody of claim 87, wherein said disease is selected from the group consisting of osteoarthritis, rheumatoid arthritis, post-traumatic osteoarthritis, idiopathic osteoarthritis, and eye disease.

89. A method of diagnosing a disease selected from the group consisting of osteoarthritis, rheumatoid arthritis, post-traumatic osteoarthritis, idiopathic osteoarthritis, and eye disease comprising contacting a sample with an antibody of claim 87.

90. The antibody of claim 83, wherein said antibody is used to detect the release of type II collagen degradation products in body fluids selected from the group consisting of tissue extracts, serum, synovial fluid, and urine.

91. A method of inhibiting chondrocyte hypertrophy in a subject comprising administering to said subject a pharmaceutically effective amount of said antibody of claim 83, whereby said hypertrophy is inhibited.

92. A method of screening for a compound capable of inhibiting collagen breakdown comprising:

- (a) incubating said test compound in vitro with an extract containing collagen;
- (b) adding a compound known to increase degradation of collagen; and
- (c) selecting said compound capable of decreasing the degradation of collagen as compared with said known compound alone.